VALVELESS MICROFLUIDIC DEVICE

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] The application claims priority under 35 U.S.C. §119 to U.S. Provisional Application Ser. No. 61/558,851, filed Nov. 11, 2011, the disclosure of which is incorporated herein by reference.

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH

[0002] This invention was made with Government support under Gran No. CHE1057113, awarded by the National Science Foundation. The Government has certain rights in this invention.

TECHNICAL FIELD

[0003] Provided are methods and devices for detecting and measuring agents. In particular, the disclosure provides methods and devices useful for detection of measurements of agents using microfluidics.

BACKGROUND

[0004] Microfluidics is a field of work that deals with the fluid-based transport of mass, momentum, or energy.

SUMMARY

[0005] The disclosure provides a valveless microfluidic system comprising a substrate; a plurality of wells located on the substrate at least one flow channel fluidly connecting each of the wells from an inlet to an outlet, each well preloaded with a desired reagent or buffer and the flow channel filled with a fluid that is immiscible with the desired reagent or buffer. In one embodiment, the fluidic system comprises a plurality of flow channels and a plurality of wells fluidly connected with each flow channel. In another embodiment, a first well of the plurality of wells comprises a magnetic bead comprising an analyte binding molecule. In another embodiment, the analyte binding molecule comprises an oligonucleotide, peptide, polypeptide, antibody or nanoparticle. In yet another embodiment, the system further comprises a magnet for moving the magnetic beads through a fluid channel, the magnet positioned relative to the substrate to provide a magnetic field that manipulates the magnetic bead. In yet another embodiment, each well comprises an aqueous material and each fluid channel comprises an oil. In another embodiment, the system further comprises a computer controller for moving the magnet relative to the substrate.

[0006] The disclosure also provides a method of purifying an analyte comprising passing an analyte through the flow channels and the plurality of wells of the microfluidic system described above and herein. In one embodiment, one or more wells of the plurality of wells comprises a purification buffer, wash buffer, lyse buffer or any combination of the foregoing for purification of the analyte. In one embodiment, the magnetic beads or moved through the fluid channels by movement of a magnet adjacent to the microfluidic device. In another embodiment, the method purifies an oligonucleotide.

[0007] The disclosure also provides a kit comprising a microfluidic system described above and elsewhere herein, preloaded with a desired combination of buffers or reagents.

[0008] The disclosure provides an integrated, droplet-based microfluidic platform for simultaneously processing a plurality of biological samples (e.g., miRNA samples). The disclosure provides a rapid and cost-effective prototyping technique, using thiolene-based optical adhesive, to fabricate microfluidic devices. A simple, but effective, syringe pump-based handling stage can be utilized for automatic or programmed operation of multiple magnetic droplets. The disclosure demonstrates the methods of the disclosure by shows miRNAs can be selectively separated from pre-miRNAs, then efficiently extracted from cell lysate matrix with high quality and eluted into RNase-free water for reliable downstream applications, such as on-chip RT reaction and in-tube real-time qPCR detection. Aside from the feasibility of on-line integration of miRNA SPE and RT(-PCR), the assay was as fast and efficient as, and more economic (~4,000%) and more flexible than the commercial kit. This microfluidic platform is also applicable for other applications, which only involve inexpensive and easily accessible equipment, and employ magnetic droplets for sample preparation and detection.

[0009] Various embodiment of the disclosure provide:

[0010] Photopolymer-based fabrication process of the microfluidic device is rapid, flexible and cost-effective, making it possible for convenient microdevice prototyping and disposable usage;

[0011] Design of the microdevice enables parallel, sample-to-answer nucleic acid analysis of multiple biological samples; higher throughput genetic analysis is possible with larger microchip substrates and more compact design with the same scheme;

[0012] The microfluidic device is compatible with regular lab equipments, such as multichannel pipette, syringe pump, PCR machine and image scanner/plate reader, which makes the operation process simple, automatic and applicable for research community;

[0013] Use of magnetic silica beads to automatically collect, fractionate, purify, and at last deliver nucleic acid samples to detection wells without intensive human operation, with the magnet fixed on a syringe pump and the chip being moved by the pump at programmed direction and speeds;

[0014] Solutions needed for sample purification and elution are pre-stored on the chip as aqueous droplets in mineral oil, minimizing further liquid handling;

[0015] Only a few microliters of samples are needed, that decreases the mass detection limit. Nucleic acid materials from a couple tens of cells are detectable.

[0016] Nucleic acid amplification is done by putting the device into a thermocycler for RT-PCR. The design is highly feasible for incorporation of an on-chip temperature control unit, and for other signaling strategies being developed in the lab, such as cation exchange for signal amplification. Both are under development in the group;

[0017] The final signal is detected by a gel imager and requires no advanced optical instruments, increasing the portability of the device and thus its compatibility with point-of-care testing.

[0018] The details of one or more embodiments are set forth in the accompanying drawings and the description below. Other features, objects, and advantages will be apparent from the description and drawings, and from the claims.